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ORIGINAL ARTICLE

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# The effects of a combined strength and aerobic exercise program on glucose control and insulin action in women with type 2 diabetes

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**Abstract** The purpose of the present study was to investigate the short- and long-term effects of a combined strength and aerobic training program on glycemic control, insulin action, exercise capacity and muscular strength in postmenopausal women with type 2 diabetes. Nine postmenopausal women, aged 55.2 (6.7) years, with type 2 diabetes participated in a supervised training program for 4 months consisting of two strength training sessions (3 sets of 12 repetitions at 60% one-repetition maximum strength) and two aerobic training sessions (60–70% of maximum heart rate at the beginning, and 70–80% of maximum heart rate after 2 months). Anthropometrical measurements, percentage glycated hemoglobin, a 2-h oral glucose tolerance test, exercise stress testing and maximum strength were measured at the beginning, and after 4 and 16 weeks of the exercise program. Significant reductions were observed in both the glucose (8.1% $P<0.01$) and insulin areas under the curve (20.7%, $P<0.05$) after 4 weeks of training. These adaptations were further improved after 16 weeks (glucose 12.5%, insulin 38%, $P<0.001$). Glycated hemoglobin was significantly decreased after 4 weeks [7.7 (1.7) vs 7.1 (1.3)%, $P<0.05$] and after 16 weeks [7.7 (1.7) vs 6.9 (1.0)%, $P<0.01$] of exercise training. Furthermore, exercise time and muscular strength were significantly improved after 4 weeks ($P<0.01$) as well as after 16 weeks ($P<0.001$) of training. Body mass and body-mass index, however, were not significantly altered throughout the study. The results indicated that a combined training program of strength and aerobic exercise could induce positive adaptations on glucose control, insulin action, muscular strength and exercise tolerance in women with type 2 diabetes.

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## Introduction

Regular exercise is established as a preventive and therapeutic treatment for chronic diseases. The metabolic effects on glucose uptake and the structural remodeling of skeletal muscle are the major reasons of the improved glucose homeostasis, even in individuals with insulin resistance diseases (Tomás et al. 2002). Concerning the type of exercise, many studies have demonstrated the positive adaptations of aerobic training on glucose control (Trovati et al. 1984; Ronnemaa et al. 1986; Wing et al. 1988; Schneider et al. 1984, 1992; Vanninen et al. 1992; Walker et al. 1999), glucose tolerance (Bogardus et al. 1984; Trovati et al. 1984; Lampman et al. 1987; Segal et al. 1991; Tessier et al. 2000) and insulin sensitivity (Bogardus et al. 1984; Trovati et al. 1984; Segal et al. 1991; Mourier et al. 1997) in patients with type 2 diabetes. Recently, however, strength training has gained popularity in exercise programs with diabetic patients due to its benefits in physical fitness and metabolic adaptations (Smutok et al. 1994; Eriksson et al. 1997; Honkola et al. 1997; Dunstan et al. 1998; Ishii et al. 1998).

Recent statements from the American Diabetes Association (2000) and the American College of Sports Medicine (2000) recommend that a complete rehabilitation program for patients with diabetes should combine both strength and aerobic exercise. Indeed, specific adaptations in skeletal muscle (Zierath 2002) seem to be beneficial to patients with type 2 diabetes, since the active muscle tissue reveals a higher metabolic rate in glucose metabolism (Baron et al. 1988).

Recently, in patients with type 2 diabetes, a well-controlled study observed that a combined strength and aerobic training program improved body composition, glucose control, cardiovascular fitness and muscular strength after 8 weeks of training (Maiorana et al. 2002). In the above study, however, only 2 of 16 patients were females. There is also a lack of data on glucose tolerance and insulin action after an exercise program that combines both strength and aerobic training for a long period of time. Therefore, the aim of the present study was to investigate the short- and long-term effects of a combined strength and aerobic exercise program on glucose tolerance, insulin sensitivity, aerobic capacity and muscular strength in postmenopausal women with type 2 diabetes.

## Methods

### Subjects

Sedentary women with type 2 diabetes were invited to take part in a regular training program. Exclusion criteria were: smoking, history of coronary artery disease, renal impairment or proteinuria, hepatic impairment, gout or hyperuricemia or uncontrolled hypertension (systolic blood pressure >160 mmHg), diabetic neuropathy or retinopathy. Nine overweight [mean (SD) body-mass index (BMI) 31.5 (3.1) kg $m^{-2}$] postmenopausal women [55.2 (6.7) years] with type 2 diabetes [percentage glycated hemoglobin (%$HbA_{1c}$) 7.7 (1.7)] agreed to participate in the study. The methods of the study were approved by the institutional ethics committee and all participants signed a written informed consent after being informed of all risks and benefits associated with the study. Seven were treated with sulfonylureas and two were subjected to dietary control. There was no alteration in the prescribed medication throughout the study. All subjects underwent comprehensive medical screening prior to participation, including medical history, physical examination and stress testing. The subjects did not participate in an exercise program for at least 6 months prior to the study, and they were instructed not to alter their diet or alcohol intake habits during the study period, and to avoid any extra exercise not included in the study training program.

### Experimental design

All subjects followed a familiarization training period of 2 weeks. Thereafter, each subject underwent anthropometric evaluation, a 2-h oral glucose tolerance test (OGTT), measurements of $HbA_{1c}$, exercise stress testing on the treadmill using the Bruce protocol, and one-repetition maximum (1-RM) strength testing on the following six exercise stations: bench press, seated row, leg extension, pull-down, pec-deck and leg curl. Afterwards, they participated in a systematic exercise program of strength and aerobic training four times per week for 16 weeks. The training program was arranged to provide an alternative day for the replacement of a possible lost session during the week. The baseline assessment was repeated after 4 and 16 weeks of training.

### Training program

#### *Aerobic training*

Aerobic exercise consisted of walking/jogging on the treadmill two times per week (Monday and Thursday). Each session lasted about 75 min including a warm-up period (5–10 min), stretching exercises (10 min), the main program with treadmill exercise (40–45 min) and a cool-down period (15 min including stretching). During the first 2 months, the intensity of aerobic exercise was 60–70% of maximum heart rate ($HR_{max}$) achieved during stress testing. Thereafter training intensity increased at 70–80% $HR_{max}$ according to the individual adaptation observed during training sessions.

#### *Strength training*

The strength training program was performed separately on non-consecutive days twice a week (Tuesday and Friday), and consisted of six resistance exercise stations: bench press, seated row, leg extension, pull-down, pec-deck and leg curl. All subjects performed 3 sets of 12 repetitions for all the exercises at an intensity of 60% 1-RM. The rest period between sets lasted 45–60 s, with 2–3 min intervals between each exercise. Weight load was applied according to the individual's ability. Each session started with a warm-up and ended with a cool-down period for 10–15 min each, including stretching.

### Testing procedures

#### *Anthropometric measurements*

Body mass and body height were measured prior to exercise test and BMI was calculated.

#### *Exercise stress testing*

All patients underwent a symptom-limited exercise test on the treadmill with ECG monitoring using the Bruce protocol. Heart rate (HR) was measured on a 12-lead electrocardiograph with an automatic ST-segment analysis, while blood pressure was recorded manually at rest and then at 3-min intervals during the stress test.

#### *Strength test*

Muscle strength was measured with the 1-RM testing method. Strength was recorded as the maximal weight

**Table 1** Alterations of anthropometric and metabolic characteristics after 4 and 16 weeks of exercise training in women with type 2 diabetes. Data are means (SD). *BMI* Body mass index, *%HbA1c* percentage glycated hemoglobin, *OGTT* oral glucose tolerance test, *AUC* area under the curve. Upper and lower body muscle strengths represent the summaries of the strength of upper and lower muscle groups, respectively

| | Baseline | 4 weeks | 16 weeks |
|---|---|---|---|
| Body mass (kg) | 81.7 (8.7) | 81.1 (7.7) | 80.5 (6.5) |
| BMI (kgm$^{-2}$) | 31.5 (3.1) | 31.3 (2.8) | 30.9 (2.6) |
| Glucose measurements | | | |
| Fasting glucose (mg dl$^{-1}$) | 144.2 (16.7) | 133.5 (14.4)$^{1*}$ | 137.1 (16.3)$^{1*}$ |
| %HbA$_{1c}$ | 7.7 (1.7) | 7.1 (1.3)$^{1*}$ | 6.9 (1.0)$^{3*}$ |
| OGTT 90 min (mg dl$^{-1}$) | 288.5 (71.4) | 263.2 (57.1) | 251.8 (49.9)$^{3*}$ |
| OGTT 120 min (mg dl$^{-1}$) | 260.8 (63.2) | 226.6 (43.3)$^{2*}$ | 220.2 (38.5)$^{3*}$ |
| Glucose AUC (g dl$^{-1}$ × min) | 32.0 (4.9) | 29.4 (4.2)$^{2*}$ | 28.0 (4.3)$^{3*}$ |
| Insulin measurements | | | |
| Fasting insulin ($\mu$U ml$^{-1}$) | 12.5 (4.9) | 11.0 (4.0) | 9.0 (3.4)$^{1*}$ |
| OGTT 90 min ($\mu$U ml$^{-1}$) | 101.6 (43.7) | 71.4 (33.5)$^{1*}$ | 62.0 (29.0)$^{3*}$ |
| OGTT 120 min ($\mu$U ml$^{-1}$) | 89.7 (32.8) | 64.2 (31.4)$^{2*}$ | 52.8 (22.0)$^{3*,4*}$ |
| Insulin AUC ($\mu$U ml$^{-1}$ × min × 10$^{3}$) | 7.7 (2.7) | 6.1 (2.8)$^{1*}$ | 4.8 (1.8)$^{3*,4*}$ |
| Exercise time (min) | 8.2 (1.2) | 9.1 (0.9)$^{2*}$ | 9.7 (0.9)$^{3*,4*}$ |
| Muscle strength | | | |
| Upper body (kg) | 150.5 (21.4) | 170.5 (22.0)$^{3*}$ | 197.8 (15.8)$^{3*,5*}$ |
| Lower body (kg) | 48.3 (10.6) | 55.2 (11.6)$^{2*}$ | 67.5 (11.1)$^{3*,5*}$ |

$^{1*}P < 0.05$, $^{2*}P < 0.01$, $^{3*}P < 0.001$, significantly different from baseline
$^{4*}P < 0.05$, $^{5*}P < 0.001$, significantly different between 4 and 16 weeks

lifted in one full range of motion, and the 1-RM was determined after either four or five trials. One minute rest followed each trial and resistance was increased by approximately 5 kg, or 2.5 kg when the patient was near to her maximum.

### *Oral glucose tolerance test*

Three days before the OGTT, all subjects consumed a minimum of 200 g of carbohydrates per day in their diet. Afterwards, following a 12-h overnight fast, a catheter was inserted in an antecubital vein and blood was drawn for analysis of HbA$_{1c}$, plasma glucose and insulin. Subjects then ingested a glucose solution [75 g (250 ml water)$^{-1}$] and subsequent blood samples were drawn at 30, 60, 90 and 120 min, and centrifuged within 30 min of collection. Blood samples were obtained 48 h after the last training session.

Plasma glucose was measured at the same time of collection using the enzymatic method of glucose oxidase (Boehringer, Biochemical Analyzer Lisa 200). Plasma samples for insulin were frozen at –80°C until later analysis. Insulin concentration was measured using a human specific radioimmunoassay kit (Diasorin, Biomedica). %HbA$_{1c}$ was measured with high-performance liquid chromatography (Menorini Pharmaceuticals). The coefficient of the variation for the HbA$_{1c}$ was below 5% in the whole measuring range.

### Statistical analysis

Data were analyzed with one-way ANOVA for repeated measures. When significant differences were revealed, the Tukey post hoc test was applied. Statistical significance was assumed for $P$ values $< 0.05$. The total area under the curve for glucose and insulin was calculated according to the trapezoidal method using both fasting concentrations and zero as the baseline.

## Results

The exercise regimen was well tolerated; no orthopedic injuries or cardiovascular complications occurred during the exercise sessions. All subjects completed the testing and training requirements of the study. The subjects in the exercise group completed all the training sessions in 4 months. There were no significant differences in anthropometric measurements throughout the study. HbA$_{1c}$ was significantly lower following 4 ($P < 0.05$) and 16 weeks of training compared to baseline ($P < 0.01$) (Table 1).

### Glucose and insulin response to OGTT

Plasma glucose concentrations decreased in the fasting state ($P < 0.05$) and at 120 min ($P < 0.01$) of the OGTT after 4 weeks of training (Fig. 1). After 16 weeks of training, glucose concentration further decreased in the fasting state and at 60 min ($P < 0.01$) as well as at 90 and 120 min ($P < 0.001$) after the oral glucose ingestion.

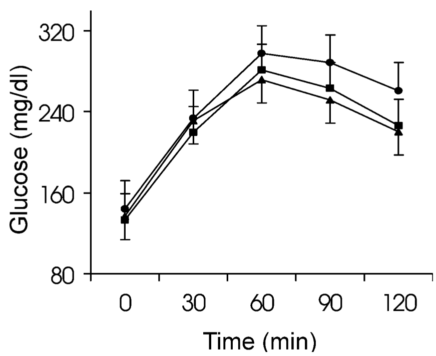


**Fig. 1** Plasma glucose concentration at fasting and after glucose challenge at baseline (●) and after 4 (■) and 16 (▲) weeks of exercise training in women with type 2 diabetes

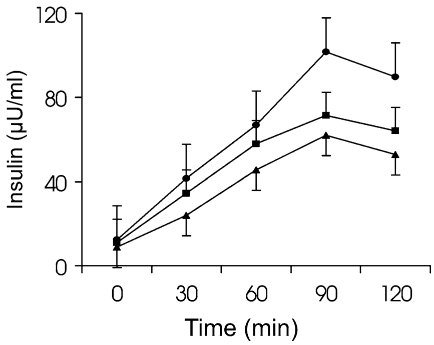


**Fig. 2** Plasma insulin concentration at fasting and after glucose challenge at baseline (●) and after 4 (■) and 16 (▲) weeks of exercise training in women with type 2 diabetes

There was an 8.1% ($P < 0.05$) and a 12.5% reduction ($P < 0.01$) in the total glucose area under the OGTT curve after 4 and 16 weeks of exercise training (Table 1). A similar pattern also occurred with insulin action (Fig. 2). In addition, the total insulin area under the OGTT curve decreased by 20.7% ($P < 0.01$) and 38% ($P < 0.001$) following 4 and 16 weeks of training, respectively (Table 1).

### Exercise capacity and muscular strength

Exercise time increased significantly after 4 weeks of training [8.2 (1.2) vs 9.1 (0.9) min, $P < 0.01$] and improved even more at the end of the study [8.2 (1.2) vs 9.7 (0.9) min, $P < 0.001$]. Favorable alterations were also found in muscular strength. Upper and lower body strength improved significantly after 4 weeks and after 16 weeks of training ($P < 0.001$; see Table 1).

## Discussion

The results of the present study demonstrated that a combined training program of strength and aerobic exercise resulted in significant improvements of glycemic control, glucose tolerance, insulin action, exercise tolerance and muscular strength in postmenopausal women with type 2 diabetes. These adaptations occurred within a period of 4 weeks of training with additional improvements observed after 16 weeks.

### Glucose tolerance and insulin sensitivity

In our study, obese females showed improvements in glucose tolerance (8.1%) and insulin sensitivity (20.7%) after 4 weeks of training, without altering their BMI significantly. A comparable study reported that 4–6 weeks of resistance exercise training (40–50% of 1-RM, five times per week) elicited a 48% improvement in insulin sensitivity (determined by hyperinsulinemic euglycemic clamp) in lean individuals with type 2 diabetes, without a significant change in maximum oxygen uptake ($\dot{V}O_{2max}$) or body composition (Ishii et al. 1998). It appears that glucose tolerance and insulin sensitivity responds independently of any changes occurring in $\dot{V}O_{2max}$ and body composition.

Glucose tolerance and insulin sensitivity further improved after 4 months of training in our patients (12.5% and 38% respectively). Similar results have been reported by other studies in which strength training alone was applied (Honkola et al. 1997; Dunstan et al. 1998, 2002; Eriksson et al. 1998). Smutok et al. (1994), in a well-controlled study with male type 2 diabetes subjects and subjects with impaired glucose tolerance or hyperinsulinemia, examined strength and aerobic exercise separately for 5 months and observed beneficial effects on glucose tolerance (12% after strength training and 16% after aerobic exercise) and insulin action (22% after strength training and 16% after aerobic exercise). In our study, however, better results were obtained with obese female subjects with type 2 diabetes. In another study, the combination of both strength and aerobic exercise proved to be an effective method of training to improve lean body mass and glycemic control in patients with type 2 diabetes (Maiorana et al. 2002).

Studies on resistance training have failed to detect improvements in $HbA_{1c}$ in patients with type 2 diabetes (Ishii et al. 1998; Dunstan et al. 1998). In those studies, the period of resistance training was less than 8 weeks at an intensity of 40–50% of maximum strength. A recent study, however, reported significant reduction in $HbA_{1c}$ at both 3 and 6 months after high intensity resistance exercise in older patients with type 2 diabetes (Dunstan et al. 2002).

Patients in our study also significantly improved their short- and long-term glycemic control. The improvement of 7.8% for $HbA_{1c}$ after 4 weeks was comparable to that observed in the study which reported a decrease of 7.1% after a combined aerobic and resistance training program of 8 weeks (Maiorana et al. 2002). Additionally in our study, $HbA_{1c}$ was further reduced by 10.4% after 4 months of training. The UK, prospective diabetes study reported that for every percentage point reduction in $HbA_{1c}$, there was a 35% reduction in microvascular complications (UK Prospective Diabetes Study 1998). Eriksson et al. (1997) also reported that a change of 7.3% in $HbA_{1c}$ following 3 months of circuit weight-training was associated with an increase in the muscle cross-sectional area (21%) in patients with type 2 diabetes, indicating the important contribution of muscle tissue to glucose metabolism. Thus, long-term glycemic control, which is required to reduce the risk of micro-vascular and macro-vascular complications, can be achieved throughout a combined strength and aerobic exercise-training program that is applied systematically and under supervision.

Adaptations in skeletal muscle, induced after aerobic exercise in diabetics (Zierath 2002; Sakamoto 2002), include improvement of $\dot{V}O_{2max}$, muscle fiber capillary density and expression of glucose transporters

(GLUT4). Exercise training also improves the activity of protein kinase $C_{-\delta}$, which has been suggested as an adaptive regulatory mechanism responsible for the enhancement of glucose uptake via GLUT4 within the muscle cell (Ryder et al. 2001) and which prevents type 2 diabetes (Heled et al. 2002). Furthermore, it has been suggested that the improved insulin sensitivity after strength training occurs via a different mechanism from that for endurance training (Poehlman et al. 2000). Recently, the increase in muscle mass induced after high-intensity strength training (75–85% of maximum strength) has been associated with improvements in glycemic control in older patients with type 2 diabetes (Dunstan et al. 2002). Therefore, the combination of both strength and aerobic exercise appears to be the appropriate mode of training for diabetic people.

## Physical performance

Strength training has gained popularity as an exercise regime for diabetic people. Maintenance of both upper and lower body muscle is important for older people to prevent falls and to accomplish daily tasks of living requiring static or dynamic efforts (Pollock et al. 2000). Our patients significantly improved their maximal strength levels in the upper (13.3%) and lower limbs (14.2%) after 4 weeks of training. These results improved further and reached values of 31.4% for the upper and 39.7% for the lower limbs after 16 weeks of training (Table 1). Other studies have also reported significant changes in muscular strength after short- (Dunstan et al. 1998; Maiorana et al. 2002) or long-term resistance training (Smutok et al. 1994; Honkola et al. 1997; Dunstan et al. 2002). In the longest follow-up study to date (5 months), strength and aerobic exercise were examined separately, and a noticeable improvement was reported in muscle strength (38% in the lower limbs and 50% in the upper limbs) for the resistance exercise group only (Smutok et al. 1994).

The patients of our study also improved their exercise tolerance by 10.9% after 4 weeks and by 18.3% after 16 weeks of training. In patients with metabolic syndrome, the combination of strength and aerobic training resulted in greater improvements of $\dot{V}O_{2max}$ than aerobic training alone (Wallace et al. 1997). This indicates that the combination of strength and aerobic training improves the overall physical fitness of the patients who need both cardiovascular endurance and muscular strength. Furthermore, increases in muscle mass, which can be better achieved after a training program including resistance exercise, have been associated with muscular fitness and glycemic control (Maiorana et al. 2002). This is due to the fact that skeletal muscles represent a large and specific target tissue for insulin action, allowing a better control of glucose levels with a greater storage of glycogen (Tesch 1988). Thus, individuals with type 2 diabetes should be encouraged to follow training programs that include both strength and aerobic exercise. Nevertheless, the physiological insight provided by resistance training alone requires further research in patients, especially in women with type 2 diabetes.

## Conclusion

The application of a specific training program that combines both strength and aerobic exercise induces positive adaptations in postmenopausal women with type 2 diabetes. These adaptations include better glycemic control, glucose tolerance and insulin action, as well as improved exercise tolerance and muscular strength. It should be pointed out that our findings are based on the characteristics of our program (supervised exercise with moderate intensity and high volume). Thus, a proper exercise program for patients with type 2 diabetes should include components that will improve cardiorespiratory fitness, muscle strength and endurance.

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